KOATE - antihemophilic factor (human)
KEDRION BIOPHARMA, INC.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use KOĀTE® safely and effectively. See full prescribing information for KOĀTE.

KOĀTE®, Antihemophilic Factor (Human)
Lyophilized Powder for Solution for Intravenous Injection
Initial U.S. Approval: 1974

INDICATIONS AND USAGE

KOĀTE is a human plasma-derived antihemophilic factor indicated for the control and prevention of bleeding episodes or in order to perform emergency and elective surgery in patients with hemophilia A (hereditary Factor VIII deficiency). (1)

Limitation of Use
KOĀTE is not indicated for the treatment of von Willebrand disease.

DOSAGE AND ADMINISTRATION

For intravenous use after reconstitution only.
- Each vial of KOĀTE contains the labeled amount of Factor VIII in international units (IU). (2)
- Required Dose (IU) = Body Weight (kg) x Desired Factor VIII Rise (IU/dL or % of normal) x 0.5
- Frequency of KOĀTE administration is determined by the type of bleeding episode and the recommendation of the treating physician.

DOSAGE FORMS AND STRENGTHS

KOĀTE is available as a lyophilized powder for reconstitution in single-use vials of 250, 500, and 1,000 international units of Factor VIII activity. (3)

CONTRAINDICATIONS

Do not use in patients who have known hypersensitivity reactions, including anaphylaxis, to KOĀTE or its components. (4)

WARNINGS AND PRECAUTIONS

- Hypersensitivity reactions, including anaphylaxis, are possible. Should symptoms occur, discontinue KOĀTE and administer appropriate treatment. (5.1)
- Development of neutralizing antibodies (inhibitors) may occur. If expected plasma Factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform an assay that measures Factor VIII inhibitor concentration. (5.2)
- Monitor for intravascular hemolysis and decreasing hematocrit values in patients with A, B or AB blood groups who are receiving large or frequent doses. (5.3)
- KOĀTE is made from human blood and therefore carries a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. (5.4)

ADVERSE REACTIONS

The most common adverse drug reactions (frequency ≥ 5% of subjects) observed in the clinical trial were nervousness, headache, abdominal pain, nausea, paresthesia and blurred vision. (6)
To report SUSPECTED ADVERSE REACTIONS, contact Grifols Therapeutics LLC at 1-800-520-2807 or FDA at 1-800-FDA-1088 or *http://www.fda.gov/medwatch*.

USE IN SPECIFIC POPULATIONS

Pediatric: clearance of Factor VIII (based on per kilogram body weight) is higher in children. Higher or more frequent dosing may be needed. (8.4)
See 17 for PATIENT COUNSELING INFORMATION.

Revised: 6/2018

FULL PRESCRIBING INFORMATION: CONTENTS*

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

1 Indications and Usage

KOĀTE® is a human plasma-derived antihemophilic factor indicated for the control and prevention of bleeding episodes or in order to perform emergency and elective surgery in patients with hemophilia A (hereditary Factor VIII deficiency).

Limitation of Use

KOĀTE is not indicated for the treatment of von Willebrand disease.

2 Dosage and Administration

For intravenous use after reconstitution only.

2.1 Dose

- Dose and duration of treatment depend on the severity of the Factor VIII deficiency, location and extent of bleeding, and the patient's clinical condition.
- Each vial of KOĀTE is labeled with the actual Factor VIII potency in international units (IU). Calculation of the required dose of Factor VIII is based on the empirical finding that one IU of Factor VIII per kg body weight raises the plasma Factor VIII activity by approximately 2% of normal activity or 2 IU/dL.

- The required dose can be determined using the following formula:

  Dose (IU) = Body Weight (kg) x Desired Factor VIII Rise (% normal or IU/dL) x 0.5

- Estimate the expected *in vivo* peak increase in Factor VIII level, expressed as IU/dL (or % normal), using the following formula:

  Estimated Increment of Factor VIII (% normal or IU/dL) = [Total Dose (IU)/Body Weight (kg)] x 2

- Patients may vary in their pharmacokinetic (e.g., half-life, in vivo recovery) and clinical responses. Base the dose and frequency on the individual clinical response.

Control and Prevention of Bleeding Episodes

A guide for dosing KOĀTE for the control and prevention of bleeding episodes (1,2) is provided in Table 1. Consideration should be given to maintaining a Factor VIII activity at or above the target range.

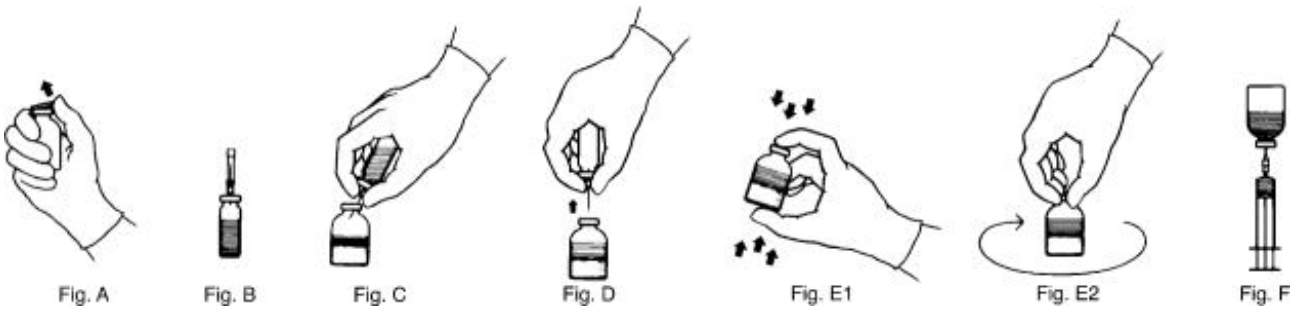
Table 1: Dosage Guidelines for Patients with Hemophilia A

Type of Bleeding	Factor VIII:C Level Required (% of normal)	Doses (IU/kg)	Frequency of Doses (hours)	Duration of Therapy (days)
Minor Large bruises Significant cuts or scrapes Uncomplicated joint hemorrhage	30	15	12 (twice daily)	Until hemorrhage stops and healing has been achieved (1–2 days).
Moderate Nose, mouth and gum bleeds Dental extractions Hematuria	50	25	12 (twice daily)	Until healing has been achieved (2–7 days, on average).
Major Joint hemorrhage Muscle hemorrhage	80-100	Initial: 40-50 Maintenance: 25	12 (twice daily)	For at least 3–5 days Until healing has been

Major trauma Hematuria Intracranial and intraperitoneal bleeding				achieved for up to 10 days. Intracranial hemorrhage may require prophylaxis therapy for up to 6 months.
Surgery	Prior to surgery: 80-100 After surgery: 60-100	40-50 30-50	Once 12 (twice daily)	Prior to surgery For the next 7–10 days, or until healing has been achieved.

2.2 Preparation and Reconstitution

1. Use aseptic technique (clean and sanitized) and a flat work surface during the reconstitution procedure.
2. Bring the vials of KOĀTE and the diluent (Sterile Water for Injection) to room temperature before use.
3. Remove the shrink band from the KOĀTE vial. Do not use KOĀTE if the shrink band is absent or shows signs of tampering, and notify Grifols Therapeutics LLC immediately.
4. Remove the plastic cap from the KOĀTE vial (Fig. A) and clean the top of the stopper with an alcohol swab. Allow the stopper to dry.
5. Repeat this step with the vial of sterile water.
6. Carefully remove the plastic sheath from the short end of the transfer needle and insert the exposed needle into the diluent vial to the hub (Fig. B)
7. Place the KOĀTE vial upright on a flat surface. Remove the sheath from the other end of the transfer needle.
8. While holding the KOĀTE vial securely on a flat surface insert the needle into the vial at a 45° angle to minimize foaming (Fig. C). The vacuum will draw the diluent into the concentrate vial. If vacuum is lost, use a sterile syringe and needle to remove the sterile water from the diluent vial and inject it into the KOĀTE, directing the stream of fluid against the wall of the vial.
9. Remove the diluent vial and transfer needle (Fig. D).
10. Agitate vigorously for 10-15 seconds, (Fig. E1) then swirl continuously until completely dissolved (Fig. E2). Avoid excessive foaming. The reconstituted solution should be clear to opalescent. Do not use if particulate matter and discoloration is observed.
11. Clean the top of the vial of reconstituted KOĀTE with alcohol swab and let surface dry.
12. Attach the filter needle (from the package) to a sterile syringe. Withdraw the KOĀTE solution into the syringe through the filter needle (Fig. F).
13. Remove the filter needle from the syringe and discard the filter needle into a puncture proof container. Use KOĀTE within 3 hours after reconstitution. Do not refrigerate after reconstitution.



2.3 Administration

For intravenous administration only

- If the dose requires more than one vial of KOĀTE:
  - Reconstitute each vial using a new transfer needle.
  - Draw up all the solution into a single syringe.
- Visually inspect the final solution for particulate matter and discoloration prior to administration, whenever solution and container permit. Do not use if particulate matter or discoloration is observed.
- Attach the syringe to the connector end of an infusion set.
- Administer intravenously. The rate of administration should be determined by the patient's comfort level, and no faster than 10 mL per minute.

3 DOSAGE FORMS AND STRENGTHS

KOĀTE is available as a lyophilized powder for reconstitution in single-use vials of 250, 500 and 1,000 IU of Factor VIII activity. The actual Factor VIII potency is labeled on each KOĀTE vial.

4 CONTRAINDICATIONS

KOĀTE is contraindicated in patients who have had hypersensitivity reactions, including anaphylaxis, to KOĀTE or its components.*[see Description (11)]*

5 WARNINGS AND PRECAUTIONS

5.1 Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, are possible. Early signs of hypersensitivity reactions, which can progress to anaphylaxis, may include angioedema, chest tightness, hypotension, rash, nausea, vomiting, paresthesia, restlessness, wheezing and dyspnea. If hypersensitivity symptoms occur, discontinue use of the product immediately and administer appropriate emergency treatment.

5.2 Neutralizing Antibodies

The formation of neutralizing antibodies (inhibitors) to Factor VIII may occur. Monitor all patients for the development of Factor VIII inhibitors by appropriate clinical observations and laboratory tests. If expected plasma Factor VIII activity levels are not attained, or if bleeding is not controlled with an appropriate dose, perform an assay that measures Factor VIII inhibitor concentration. *[see Warnings and Precautions (5.5)]*

5.3 Intravascular Hemolysis

KOĀTE contains blood group isoagglutinins which are not clinically significant when small doses are used to treat minor bleeding episodes. However, when large and/or frequent doses of KOĀTE are given to patients with blood groups A, B, or AB, acute hemolytic anemia may occur, resulting in

increased bleeding tendency or hyperfibrinogenemia. Monitor these patients for signs of intravascular hemolysis and falling hematocrit. *[see* Warnings and Precautions (5.5)*]* Should this condition occur, leading to progressive hemolytic anemia, discontinue KOĀTE and consider administering serologically compatible Type O red blood cells and providing alternative therapy.

5.4 Transmissible Infectious Agents

Because KOĀTE is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent and, theoretically, the Creutzfeldt-Jakob disease (CJD) agent. There is also the possibility that unknown infectious agents may be present in the product. The risk that the product will transmit viruses has been reduced by screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and removing certain viruses during manufacture. Despite these measures, this product may still potentially transmit diseases.

Report all infections suspected by a physician possibly to have been transmitted by this product to Grifols Therapeutics LLC at 1-800-520-2807.

5.5 Monitoring: Laboratory Tests

- Monitor plasma Factor VIII activity levels by performing a validated test (e.g., one-stage clotting assay) to confirm that adequate Factor VIII levels have been achieved and maintained. *[see* Dosage ad Administration (2.1)*]*
- Monitor for the development of Factor VIII inhibitors. Perform a Bethesda inhibitor assay if expected Factor VIII plasma levels are not attained, or if bleeding is not controlled with the expected dose of KOĀTE. Use Bethesda Units (BU) to report inhibitor levels.
- Monitor for intravascular hemolysis and decreasing hematocrit values in patients with A, B or AB blood groups who are receiving large or frequent doses of KOĀTE.

6 ADVERSE REACTIONS

The most common adverse drug reactions (frequency ≥ 5 % of subjects) observed in the clinical trial were nervousness, headache, abdominal pain, nausea, paresthesia and blurred vision.

6.1 Clinical Trials Experience

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed cannot be directly compared to rates in other clinical trials and may not reflect the rates observed in practice.

The safety assessment of KOĀTE is based on data from a 2-stage, safety, pharmacokinetic (PK) and efficacy clinical trial in which twenty subjects with severe hemophilia A (<1% endogenous Factor VIII activity) were evaluable for safety. Nineteen subjects were enrolled in Stage I of the trial, including 15 Caucasian, 3 Hispanic, and 1 Black subjects. The mean age was 29 years (range: 13.9 – 46.4 years). Nineteen subjects, including the 18 subjects who completed Stage I, and one new subject were enrolled in Stage II. The mean age was 30 years (range: 13.9 – 46.4). The subjects received a total of 1053 infusions. Ten adverse reactions related to 7 infusions were reported in 4 subjects. These were: nervousness (2 subjects [10%]), headache (1 subject [5%]), abdominal pain (1 subject [5%]), nausea (1 subject [5%]), paresthesia (1 subject [5%]), and blurred vision (1 subject [5%]).

Immunogenicity

Subjects were monitored for neutralizing antibodies (inhibitors) to Factor VIII by the Bethesda assay at baseline and at 8, 17 and 26 weeks. No evidence of inhibitor formation was observed in the clinical trial.

The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay

may be influenced by several factors including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, it may be misleading to compare the incidence of antibodies to KOĀTE in the study described above with the incidence of antibodies in other studies or to other products.

6.2 Postmarketing Experience

Because postmarketing reporting of adverse reactions is voluntary and from a population of uncertain size, it is not always possible to reliably estimate the frequency of these reactions or establish a causal relationship to product exposure.

- Blood and Lymphatic System Disorders: Factor VIII inhibition, hemolytic anemia
- Immune System Disorders: Hypersensitivity including anaphylaxis, rash, pruritus
- Injury, Poisoning and Procedural Complications: Post-procedural hemorrhage
- Nervous System Disorders: Generalized clonic-tonic seizure

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no data with KOĀTE use in pregnant women to inform on drug-associated risk. Animal reproduction studies have not been conducted using KOĀTE. It is not known whether KOĀTE can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. KOĀTE should be given to a pregnant woman only if clearly needed. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

8.2 Lactation

Risk Summary

There is no information regarding the presence of KOĀTE in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for KOĀTE and any potential adverse effects on the breast-fed infant from KOĀTE or from the underlying maternal condition.

8.4 Pediatric Use

Safety and efficacy studies have been performed in 20 previously treated pediatric patients aged 2.5 to 16 years. Subjects received 208 infusions of KOĀTE for treatment or control of bleeding episodes, including perioperative management, and routine prophylaxis. Children have shorter half-life and lower recovery of Factor VIII than adults. Because clearance of Factor VIII (based on per kilogram body weight) is higher in children, higher or more frequent dosing may be needed.

8.5 Geriatric Use

Clinical studies of KOĀTE did not include any subjects aged 65 and over to determine whether they respond differently from younger subjects. Individualize dose selection for geriatric patients.

11 DESCRIPTION

KOĀTE, Antihemophilic Factor (Human), is a sterile, stable, dried concentrate of human antihemophilic factor in lyophilized powder form for reconstitution for intravenous injection. The product is supplied in single-use vials containing nominally 250, 500, or 1,000 international units (IU or units). Each vial of KOĀTE is labeled with the actual amount of Factor VIII expressed in IU. One IU is defined by the

current World Health Organization International Standard for Factor VIII concentrate, which can be traced to the level of Factor VIII found in 1 mL of fresh pooled human plasma. The final product when reconstituted as directed contains not more than (NMT) 1500 µg/mL polyethylene glycol (PEG), NMT 0.05 M glycine, NMT 25 µg/mL polysorbate 80, NMT 5 µg/g tri-n-butyl phosphate (TNBP), NMT 3 mM calcium, NMT 1 µg/mL aluminum, NMT 0.06 M histidine, and NMT 10 mg/mL human albumin.

KOĀTE is purified from the cold insoluble fraction of pooled human plasma; the manufacturing process includes solvent/detergent (TNBP and polysorbate 80) treatment and heat treatment of the lyophilized final container. A gel permeation chromatography step serves the dual purpose of reducing the amount of TNBP and polysorbate 80 as well as increasing the purity of the Factor VIII in KOĀTE to 300 to 1,000 times over whole plasma. When reconstituted as directed, KOĀTE contains approximately 50 to 150 times as much Factor VIII as an equal volume of fresh plasma. The specific activity after addition of human albumin is in the range of 9 to 22 units/mg protein. KOĀTE also contains naturally occurring von Willebrand factor, which is co-purified as part of the manufacturing process.

The KOĀTE manufacturing process includes two dedicated steps with virus inactivation capacity. The solvent/detergent treatment step has the capacity to inactivate enveloped viruses (such as HIV, HCV, HBV, and WNV). Heat treatment at 80°C for 72 hours has the capacity to inactivate enveloped viruses (such as HIV and HCV) as well as non‑enveloped viruses (such as HAV and B19V). The polyethylene glycol (PEG) precipitation/depth filtration step has the capacity to remove both enveloped and non‑enveloped viruses. The accumulated virus reduction factors for KOĀTE manufacturing process are presented in Table 2.

Table 2: Virus Clearance Capacity (Log_{10}) for the Antihemophilic Factor (Human) Manufacturing Process

	Enveloped Viruses					**Non-enveloped Viruses**		
	HIV-1	**BVDV**	**PRV**	**VSV**	**WNV**	**Reo3**	**HAV**	**PPV**
Model for	HIV-1/2	HCV	Large enveloped DNA viruses (e.g., herpes virus)	Enveloped RNA viruses	WNV	Non-enveloped viruses	HAV	B19V
Global Reduction Factor	≥ 12.0	≥ 11.5	≥ 10.8	≥ 10.9	≥ 5.9*	≥ 9.9	≥ 5.5	4.8
* WNV inactivation was evaluated only for the solvent/detergent treatment step								

Additionally, the manufacturing process was investigated for its capacity to decrease the infectivity of an experimental agent of transmissible spongiform encephalopathy (TSE), considered a model for the variant Creutzfeldt-Jakob disease (vCJD) and Creutzfeldt-Jakob disease (CJD) agents. The manufacturing process has been shown to decrease TSE infectivity of that experimental model agent (a total of 5.1 log_{10} reduction), providing reasonable assurance that low levels of vCJD/CJD agent infectivity, if present in the starting material, would be removed.

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

KOĀTE temporarily replaces the missing clotting Factor VIII that is needed for effective hemostasis.

12.2 Pharmacodynamics

Hemophilia A is a bleeding disorder characterized by a deficiency of functional coagulation Factor VIII, resulting in a prolonged plasma clotting time as measured by the activated partial thromboplastin time (aPTT) assay. Treatment with KOĀTE normalizes the aPTT over the effective dosing period.

12.3 Pharmacokinetics

The pharmacokinetics (PK) of KOĀTE were evaluated in a prospective, two-stage clinical trial of 20 previously treated patients (PTPs) with severe hemophilia A. In Stage I, the PK parameters for 19 subjects were based on plasma Factor VIII activity after a single intravenous infusion of 50 IU/kg of KOĀTE. Bioequivalence of the dry heat-treated KOĀTE to the unheated KOĀTE was demonstrated by comparison of C_{max} and the area under the curve, AUC_{0-48} (Table 3). The incremental *in vivo* recovery ten minutes after infusion of dry heat-treated KOĀTE was 1.90% unit/kg (unheated KOĀTE was 1.82% units/kg). Mean biologic half-life was 16.1 hours.

In Stage II of the study, participants received KOĀTE treatments for six months on home therapy with a median of 52 days (range 23 to 94 days). At the end of 6 months, the mean AUC_{0-48} was 1471 ± 237 unit*hour/100 mL, the C_{max} was 99 ± 13 unit/100 mL, and the $t_{1/2}$was 16 ± 3.9 hours.

Table 3: PK Parameters of KOĀTE (Stage I of Crossover Trial)

Parameter	KOĀTE Dry Heat-treated (mean ± SD)	KOĀTE Unheated (mean ± SD)
AUC_{0-48}(IU hr/mL))	1432 ±288	1477 ± 343
C_{max}(IU/mL)	103 ± 19	99 ± 20
T_{max}(hr)	0.41 ± 0.26	0.43 ± 0.44
Half life (hr)	16.1 ± 3.2	16.1 ± 5.1

14 CLINICAL STUDIES

The efficacy of KOĀTE for the treatment of bleeding episodes was demonstrated in a 2-stage, safety, PK and efficacy clinical trial. Stage I was a randomized, single-blind, single-dose, crossover, and PK study comparing heat-treated KOĀTE with unheated KOĀTE. Nineteen subjects were randomized and received a single dose of 50 IU/kg of either heated KOĀTE or unheated KOĀTE for PK assessment. Stage II was a 6 month open-label safety study conducted at two hemophilia centers. Nineteen subjects received KOĀTE, including for on-demand treatment and control of bleeding episodes. The study populations included 15 Caucasians, 3 Hispanic, and 1 Black subject. A total of 306 bleeding episodes were treated, of which 82% were treated with a single infusion of Factor VIII.

15 REFERENCES

1. Srivastava A, Brewer AK, Mauser-Bunschoten EP, et al. Guidelines for the management of hemophilia. Haemophilia 2013;19(1):e1-47.
2. Abildgaard CF. Current concepts in the management of hemophilia. Semin Hematol 1975;12(3):223-32.

16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

KOĀTE is supplied in single-use vials containing 250, 500 or 1,000 IU of Factor VIII activity, packaged with 5 mL or 10 mL of Sterile Water for Injection, one sterile double-ended transfer needle, one sterile filter needle, and one sterile administration set. The actual amount of KOĀTE in IU is stated on each carton and vial label.

Components used in the packaging of KOĀTE are not made with natural rubber latex.

Strength	NDC Number Carton (Kit)
250 IU	76125-250-20 or 76125-253-25
500 IU	76125-667-30 or 76125-662-50
1,000 IU	76125-672-50 or 76125-674-10

Storage and Handling

- Store KOĀTE in its original package to protect it from light.
- Store the KOĀTE package at 2 to 8°C (36 to 46°F). Do not freeze.
- KOĀTE may also be stored at room temperature (up to 25°C or 77°F) for up to 6 months.
- Do not use after the expiration date.
- Use reconstituted KOĀTE immediately or within 3 hours of reconstitution.

17 PATIENT COUNSELING INFORMATION

- Inform patients to immediately report the following early signs and symptoms of hypersensitivity reactions to their healthcare professional: angioedema, chest tightness, hypotension, rash, nausea, vomiting, paresthesia, restlessness, wheezing and dyspnea. *[see Warnings and Precautions (5.1)]*
- Inform patients that the development of inhibitors to Factor VIII is a possible complication of treatment with KOĀTE. Advise the patients to contact their healthcare provider for further treatment and/or assessment if they experience a lack of clinical response to KOĀTE because this may be a manifestation of an inhibitor. *[see Warnings and Precautions (5.2)]*
- Inform patients that KOĀTE is made from human plasma and may carry a risk of transmitting infectious agents. While the risk that KOĀTE can transmit an infection has been reduced by screening plasma donors for prior exposure, testing donated plasma, and inactivating or removing certain viruses during manufacturing, patients should report any symptoms that concern them. *[see Warnings and Precautions (5.4)*

Manufactured for:
Kedrion Biopharma Inc.
400 Kelby Street
Fort Lee, NJ 07024

Manufactured by:
Grifols Therapeutics LLC
Research Triangle Park, NC 27709 USA
US License No. 1871

3036433

PACKAGE LABEL PRINCIPAL DISPLAY PANEL

NDC 76125-252-21

Koāte®

Antihemophilic Factor (Human)

Solvent/Detergent Treated

Heat-Treated at 80°C

Manufactured for:
Kedrion Biopharma Inc.
400 Kelby Street, Fort Lee, NJ 07024

Manufactured by:
Grifols Therapeutics LLC
Research Triangle Park, NC 27709 USA
U.S. License No. 1871

The patient and physician should discuss the risks and benefits of this product.

No Preservative

For Intravenous Administration Only

Sterile—Nonpyrogenic

Reconstitute with 5 mL Sterile Water for Injection, USP.

Store at 2–8°C (36–46°F) and no more than 6 months at room temperature (up to 25°C; 77°F) at any time prior to the expiration date.

Dosage and Administration: Read package insert.

Rx only

Date removed from refrigeration_____

Lot

Exp.

IU

3051798

NDC 13533-000-04

3053017

Nonpyrogenic

Single-Dose Container

5 mL

Sterile Water for Injection, USP
for reconstitution of accompanying product

Do not use unless clear. No antimicrobial agent or other substance has been added. Do not use for intravascular injection without making approximately isotonic by addition of suitable solute. Discard unused portion.

Rx Only.

Mfd by: **Baxter Healthcare Corporation**
Deerfield, IL 60015 USA

Mfd for: **Grifols Therapeutics LLC**
Research Triangle Park, NC 27709 USA

07-32-00-0008

Lot
Exp.

NDC 76125-250-20

Koāte®
Antihemophilic Factor (Human)

250 IU FVIII Range

Solvent/Detergent Treated

Heat-Treated at 80°C

5 mL

Rx only

CONTENTS:
One bottle of Koāte
5 mL Sterile Water for Injection, USP
One sterile filter needle
One sterile double-ended transfer needle
One sterile administration set

No Preservative

For Intravenous Administration Only

Sterile — Nonpyrogenic

Date removed from refrigeration_____

WARNING: THIS PRODUCT IS PREPARED FROM LARGE POOLS OF HUMAN PLASMA WHICH MAY CARRY THE RISK OF TRANSMITTING INFECTIOUS AGENTS.

The patient and physician should discuss the risks and benefits of this product.

Dosage and Administration: Read enclosed package insert.

Store refrigerated at 2 to 8°C (36 to 46°F) and no more than 6 months at room temperature (up to 25°C; 77°F) at any time prior to the expiration date. Avoid freezing.

Reconstitute with 5 mL Sterile Water for Injection, USP.

Administer within 3 hours after reconstitution.

This product when reconstituted contains not more than (NMT) 1500 µg/mL polyethylene glycol (PEG), NMT 0.05 M glycine, NMT 25 µg/mL polysorbate 80, NMT 5 µg/g tri-n-butyl phosphate (TNBP), NMT 3 mM calcium, NMT 1 µg/mL aluminum, NMT 0.06 M histidine, and NMT 10 mg/mL Albumin (Human).

If the shrink band is absent or shows any sign of tampering, do not use the product and notify Grifols Therapeutics LLC immediately.

Not Returnable for Credit or Exchange

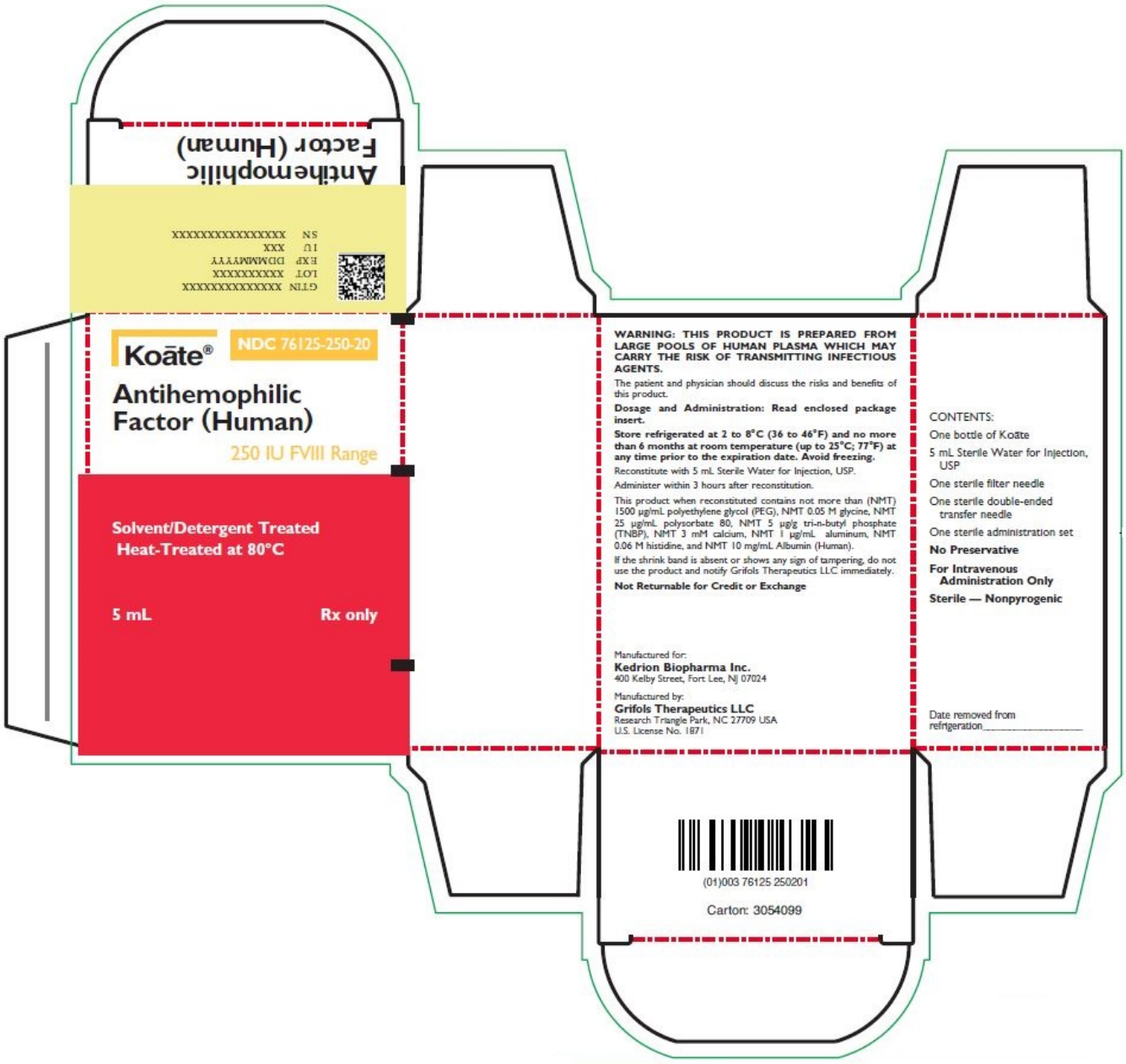
Manufactured for:
Kedrion Biopharma Inc.
400 Kelby Street, Fort Lee, NJ 07024

Manufactured by:
Grifols Therapeutics LLC
Research Triangle Park, NC 27709 USA

U.S. License No. 1871

GTIN XXXXXXXXXXXXXX
LOT XXXXXXXXXX
EXP DDMMMYYYY
IU XXX
SN XXXXXXXXXXXXXXX

Carton: 3054099



NDC 76125-669-31

Koāte®

Antihemophilic Factor (Human)

Solvent/Detergent Treated

Heat-Treated at 80°C

Manufactured for:
Kedrion Biopharma Inc.
400 Kelby Street, Fort Lee, NJ 07024

Manufactured by:
Grifols Therapeutics LLC

Research Triangle Park, NC 27709 USA
U.S. License No. 1871

The patient and physician should discuss the risks and benefits of this product.

No Preservative

For Intravenous Administration Only

Sterile—Nonpyrogenic

Reconstitute with 5 mL Sterile Water for Injection, USP.

Store at 2–8°C (36–46°F) and no more than 6 months at room temperature (up to 25°C; 77°F) at any time prior to the expiration date.

Dosage and Administration: Read package insert.

Rx only

Date removed from refrigeration_____

Lot

Exp.

IU

3051807

NDC 76125-667-30

Koāte®
Antihemophilic Factor (Human)

500 IU FVIII Range

Solvent/Detergent Treated

Heat-Treated at 80°C

5 mL

Rx only

CONTENTS:
One bottle of Koāte
5 mL Sterile Water for Injection, USP
One sterile filter needle
One sterile double-ended transfer needle
One sterile administration set

No Preservative

For Intravenous Administration Only

Sterile — Nonpyrogenic

Date removed from refrigeration_____

WARNING: THIS PRODUCT IS PREPARED FROM LARGE POOLS OF HUMAN PLASMA WHICH MAY CARRY THE RISK OF TRANSMITTING INFECTIOUS AGENTS.

The patient and physician should discuss the risks and benefits of this product.

Dosage and Administration: Read enclosed package insert.

Store refrigerated at 2 to 8°C (36 to 46°F) and no more than 6 months at room temperature (up to 25°C; 77°F) at any time prior to the expiration date. Avoid freezing.

Reconstitute with 5 mL Sterile Water for Injection, USP.

Administer within 3 hours after reconstitution.

This product when reconstituted contains not more than (NMT) 1500 µg/mL polyethylene glycol (PEG), NMT 0.05 M glycine, NMT 25 µg/mL polysorbate 80, NMT 5 µg/g tri-n-butyl phosphate (TNBP), NMT 3 mM calcium, NMT 1 µg/mL aluminum, NMT 0.06 M histidine, and NMT 10 mg/mL Albumin (Human).

If the shrink band is absent or shows any sign of tampering, do not use the product and notify Grifols Therapeutics LLC immediately.

Not Returnable for Credit or Exchange

Manufactured for:
Kedrion Biopharma Inc.
400 Kelby Street, Fort Lee, NJ 07024

Manufactured by:

Grifols Therapeutics LLC
Research Triangle Park, NC 27709 USA

U.S. License No. 1871

GTIN XXXXXXXXXXXXXX
LOT XXXXXXXXXX
EXP DDMMMYYYY
IU XXX
SN XXXXXXXXXXXXXXXX

Carton: 3054100

NDC 76125-673-51

Koāte®

Antihemophilic Factor (Human)

Solvent/Detergent Treated

Heat-Treated at 80°C

Manufactured for:
Kedrion Biopharma Inc.
400 Kelby Street, Fort Lee, NJ 07024

Manufactured by:
Grifols Therapeutics LLC
Research Triangle Park, NC 27709 USA
U.S. License No. 1871

The patient and physician should discuss the risks and benefits of this product.

No Preservative

For Intravenous Administration Only

Sterile—Nonpyrogenic

Reconstitute with 10 mL Sterile Water for Injection, USP.

Store at 2–8°C (36–46°F) and no more than 6 months at room temperature (up to 25°C; 77°F) at any time prior to the expiration date.

Dosage and Administration: Read package insert.

Rx only

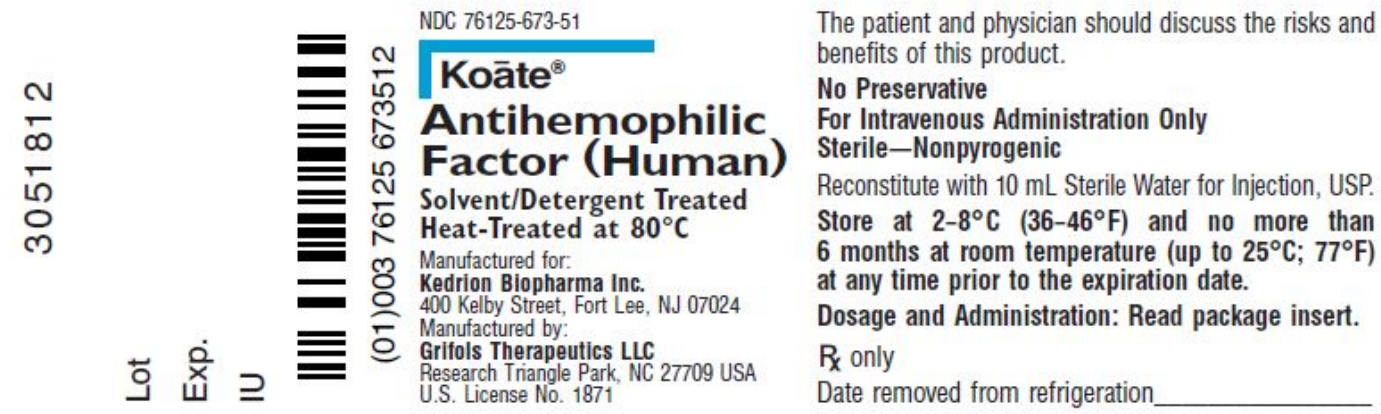
Date removed from refrigeration_____

Lot

Exp.

IU

3051812



NDC 76125-672-50

Koāte®
Antihemophilic Factor (Human)

1000 IU FVIII Range

Solvent/Detergent Treated

Heat-Treated at 80°C

10 mL

Rx only

CONTENTS:
One bottle of Koāte
10 mL Sterile Water for Injection, USP
One sterile filter needle
One sterile double-ended transfer needle
One sterile administration set

No Preservative

For Intravenous Administration Only

Sterile — Nonpyrogenic

Date removed from refrigeration_____

WARNING: THIS PRODUCT IS PREPARED FROM LARGE POOLS OF HUMAN PLASMA WHICH MAY CARRY THE RISK OF TRANSMITTING INFECTIOUS AGENTS.

The patient and physician should discuss the risks and benefits of this product.

Dosage and Administration: Read enclosed package insert.

Store refrigerated at 2 to 8°C (36 to 46°F) and no more than 6 months at room temperature (up to 25°C; 77°F) at any time prior to the expiration date. Avoid freezing.

Reconstitute with 10 mL Sterile Water for Injection, USP.

Administer within 3 hours after reconstitution.

This product when reconstituted contains not more than (NMT) 1500 µg/mL polyethylene glycol (PEG), NMT 0.05 M glycine, NMT 25 µg/mL polysorbate 80, NMT 5 µg/g tri-n-butyl phosphate (TNBP), NMT 3 mM calcium, NMT 1 µg/mL aluminum, NMT 0.06 M histidine, and NMT 10 mg/mL Albumin (Human).

Not Returnable for Credit or Exchange

Manufactured for:
Kedrion Biopharma Inc.
400 Kelby Street, Fort Lee, NJ 07024

Manufactured by:
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Research Triangle Park, NC 27709 USA

U.S. License No. 1871

GTIN XXXXXXXXXXXXXX
LOT XXXXXXXXXX
EXP DDMMMYYYY
IU XXX
SN XXXXXXXXXXXXXXX

Carton:3054101

NDC 13533-000-05

3053018

Nonpyrogenic

Single-Dose Container

10 mL

Sterile Water for Injection, USP
for reconstitution of accompanying product

Do not use unless clear. No antimicrobial agent or other substance has been added. Do not use for intravascular injection without making approximately isotonic by addition of suitable solute. Discard unused portion.

Rx Only.

Mfd by: **Baxter Healthcare Corporation**

Deerfield, IL 60015 USA

Mfd for: **Grifols Therapeutics LLC**
Research Triangle Park, NC 27709 USA

07-32-00-0009

Lot
Exp.

-

KOATE

antihemophilic factor (human) kit

Product Information			
Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:76125-250

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:76125-250-20	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL, GLASS	5 mL
Part 2	1 VIAL, GLASS	5 mL

Part 1 of 2

KOATE

antihemophilic factor (human) injection, powder, lyophilized, for solution

Product Information	
Item Code (Source)	NDC:76125-252
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Antihemophilic Factor Human (UNII: 839MOZ74GK) (Antihemophilic Factor Human - UNII:839MOZ74GK)	Antihemophilic Factor Human	250 [iU] in 5 mL

Inactive Ingredients	
Ingredient Name	**Strength**
Albumin Human (UNII: ZIF514RVZR)	
Sodium Chloride (UNII: 451W47IQ8X)	
Histidine (UNII: 4QD397987E)	
Calcium Chloride (UNII: M4I0D6VV5M)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:76125-252-21	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Part 2 of 2

STERILE WATER

water injection

Product Information	
Item Code (Source)	NDC:13533-000
Route of Administration	INTRAVENOUS

Inactive Ingredients	
Ingredient Name	**Strength**

Water (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:13533-000-04	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

KOATE

antihemophilic factor (human) kit

Product Information

Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:76125-253

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-253-25	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, GLASS	5 mL
Part 2	1 VIAL, GLASS	5 mL

Part 1 of 2

KOATE

antihemophilic factor (human) injection, powder, lyophilized, for solution

Product Information

Item Code (Source)	NDC:76125-252
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Antihemophilic Factor Human (UNII: 839MOZ74GK) (Antihemophilic Factor Human - UNII:839MOZ74GK)	Antihemophilic Factor Human	250 [iU] in 5 mL

Inactive Ingredients

Ingredient Name	Strength
Albumin Human (UNII: ZIF514RVZR)	
Sodium Chloride (UNII: 451W47IQ8X)	
Histidine (UNII: 4QD397987E)	
Calcium Chloride (UNII: M4I0D6VV5M)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-252-21	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Part 2 of 2

STERILE WATER

water injection

Product Information

Item Code (Source)	NDC:13533-200
Route of Administration	INTRAVENOUS

Inactive Ingredients

Ingredient Name	Strength
Water (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date

1	NDC:13533-200-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

KOATE

antihemophilic factor (human) kit

Product Information

Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:76125-667

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-667-30	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, GLASS	5 mL
Part 2	1 VIAL, GLASS	5 mL

Part 1 of 2

KOATE

antihemophilic factor (human) injection, powder, lyophilized, for solution

Product Information

Item Code (Source)	NDC:76125-669
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Antihemophilic Factor Human (UNII: 839MOZ74GK) (Antihemophilic Factor Human - UNII:839MOZ74GK)	Antihemophilic Factor Human	500 [iU] in 5 mL

Inactive Ingredients

Ingredient Name	Strength
Albumin Human (UNII: ZIF514RVZR)	
Sodium Chloride (UNII: 451W47IQ8X)	
Histidine (UNII: 4QD397987E)	
Calcium Chloride (UNII: M4I0D6VV5M)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-669-31	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Part 2 of 2

STERILE WATER

water injection

Product Information

Item Code (Source)	NDC:13533-000
Route of Administration	INTRAVENOUS

Inactive Ingredients

Ingredient Name	Strength
Water (UNII: 059QF0KO0R)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:13533-000-04	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

KOATE

antihemophilic factor (human) kit

Product Information

Product Type	PLASMA DERIVATIVE	Item Code (Source)	NDC:76125-662

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-662-50	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, GLASS	5 mL
Part 2	1 VIAL, GLASS	5 mL

Part 1 of 2

KOATE

antihemophilic factor (human) injection, powder, lyophilized, for solution

Product Information

Item Code (Source)	NDC:76125-669
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Antihemophilic Factor Human (UNII: 839MOZ74GK) (Antihemophilic Factor Human - UNII:839MOZ74GK)	Antihemophilic Factor Human	500 [iU] in 5 mL

Inactive Ingredients	
Ingredient Name	**Strength**
Albumin Human (UNII: ZIF514RVZR)	
Sodium Chloride (UNII: 451W47IQ8X)	
Histidine (UNII: 4QD397987E)	
Calcium Chloride (UNII: M4I0D6VV5M)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:76125-669-31	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	**Application Number or Monograph Citation**	**Marketing Start Date**	**Marketing End Date**
BLA	BLA101130	05/20/1999	

Part 2 of 2

STERILE WATER

water injection

Product Information	
Item Code (Source)	NDC:13533-200
Route of Administration	INTRAVENOUS

Inactive Ingredients	
Ingredient Name	**Strength**
Water (UNII: 059QF0KO0R)	

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:13533-200-05	5 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	**Application Number or Monograph Citation**	**Marketing Start Date**	**Marketing End Date**
BLA	BLA101130	05/20/1999	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

KOATE

antihemophilic factor (human) kit

Product Information

Product Type	PLASMA DERIVATIVE	Item Code (Source)	NDC:76125-672

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-672-50	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts

Part #	Package Quantity	Total Product Quantity
Part 1	1 VIAL, GLASS	10 mL
Part 2	1 VIAL, GLASS	10 mL

Part 1 of 2

KOATE

antihemophilic factor (human) injection, powder, lyophilized, for solution

Product Information

Item Code (Source)	NDC:76125-673
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety

Ingredient Name	Basis of Strength	Strength
Antihemophilic Factor Human (UNII: 839MOZ74GK) (Antihemophilic Factor Human - UNII:839MOZ74GK)	Antihemophilic Factor Human	1000 [iU] in 10 mL

Inactive Ingredients

Ingredient Name	Strength
Albumin Human (UNII: ZIF514RVZR)	
Sodium Chloride (UNII: 451W47IQ8X)	

Histidine (UNII: 4QD397987E)	
Calcium Chloride (UNII: M4I0D6VV5M)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-673-51	10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Part 2 of 2

STERILE WATER

water injection

Product Information	
Item Code (Source)	NDC:13533-000
Route of Administration	INTRAVENOUS

Inactive Ingredients	
Ingredient Name	Strength
Water (UNII: 059QF0KO0R)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:13533-000-05	10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date

BLA	BLA101130	05/20/1999	

KOATE

antihemophilic factor (human) kit

Product Information			
Product Type	PLASMA DERIVATIVE	**Item Code (Source)**	NDC:76125-674

Packaging				
#	**Item Code**	**Package Description**	**Marketing Start Date**	**Marketing End Date**
1	NDC:76125-674-10	1 in 1 CARTON; Type 9: Other Type of Part 3 Combination Product (e.g., Drug/Device/Biological Product)		

Quantity of Parts		
Part #	**Package Quantity**	**Total Product Quantity**
Part 1	1 VIAL, GLASS	10 mL
Part 2	1 VIAL, GLASS	10 mL

Part 1 of 2

KOATE

antihemophilic factor (human) injection, powder, lyophilized, for solution

Product Information	
Item Code (Source)	NDC:76125-673
Route of Administration	INTRAVENOUS

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Antihemophilic Factor Human (UNII: 839MOZ74GK) (Antihemophilic Factor Human - UNII:839MOZ74GK)	Antihemophilic Factor Human	1000 [iU] in 10 mL

Inactive Ingredients	
Ingredient Name	**Strength**
Albumin Human (UNII: ZIF514RVZR)	
Sodium Chloride (UNII: 451W47IQ8X)	
Histidine (UNII: 4QD397987E)	
Calcium Chloride (UNII: M4I0D6VV5M)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:76125-673-51	10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Part 2 of 2

STERILE WATER

water injection

Product Information	
Item Code (Source)	NDC:13533-200
Route of Administration	INTRAVENOUS

Inactive Ingredients	
Ingredient Name	Strength
Water (UNII: 059QF0KO0R)	

Packaging				
#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:13533-200-10	10 mL in 1 VIAL, GLASS; Type 0: Not a Combination Product		

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Marketing Information			
Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
BLA	BLA101130	05/20/1999	

Labeler - KEDRION BIOPHARMA, INC. (078622209)

Establishment

Name	Address	ID/FEI	Business Operations
GRIFOLS THERAPEUTICS LLC		611019113	manufacture(76125-250, 76125-253, 76125-662, 76125-667, 76125-672, 76125-674)

Revised: 1/2020 KEDRION BIOPHARMA, INC.